DETAILED ACTION

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/05/2010 has been entered.

Status of Application/Amendment/Claims

Applicant's response 10/05/2010 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 02/18/2010 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

With entry of the amendment filed on 02/18/2010, claims 1, 4-6, 10, 13 and 14 are pending in the application.

New Claim Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 5, 6, 10 and 13-14 are rejected under 35 U.S.C. 102(e) as being anticipated by Fosnaugh et al. (US 2003/0143732 of record) as evidenced by Thierry et al. (US 6,110,490 of record).

The instant claims are drawn to a composition for delivering an RNA to a cell comprising a reversibly modified RNA consisting of a hydrophobic group covalently linked to said RNA via a labile bond cleavable under mammalian physiological conditions and an amphipathic transfection reagent wherein the reversibly modified RNA and the transfection reagent associate to form a complex and wherein the modified RNA interacts with the transfection reagent via hydrophobic interactions and drawn to a RNA that is modified and is selected from siRNA or microRNA, wherein the modified RNA is more resistant to nucleases and wherein a plurality of functional groups are attached to said RNA via labile bonds.

Fosnaugh et al. teach conjugates comprising siRNA and functional groups that are used to facilitate delivery of the siRNA into cells (see paragraph 0172). Fosnaugh

et al. teach the siRNA can be modified at the 2' hydroxyl position (see paragraph 0165) and teach the functional groups are attached to the siRNA via biodegradable linkers wherein the linkers are degradable in biological systems i.e. mammalian cells (see paragraph 0174). Fosnaugh et al. teach the functional groups can be lipids, peptides, toxins or polymers that are capable of delivering the siRNA across cellular membranes, (see paragraphs 0172- 0175). Moreover, Fosnaugh et al. teach the conjugate can be delivered to an individual using liposomal delivery and teach standard protocols can be used for formation of the liposome complex (see at least paragraph 0195). As evidenced by Thierry et al., liposomal complexes comprising oligonucleotides are formed by hydrophobic interactions (see generally columns 8-11).

Because Fosnaugh et al. teach a composition comprising a modified RNA and an amphipathic transfection reagent as claimed, the claimed properties or functions are presumed to be inherent per the MPEP cited below.

The MPEP states:

A REFERENCE TEACHING PRODUCT APPEARING TO BE SUBSTANTIALLY IDENTICAL IS MADE THE BASIS OF A REJECTION, AND THE EXAMINER PRESENTS EVIDENCE OR REASONING TENDING TO SHOW INHERENCY, THE BURDEN SHIFTS TO THE APPLICANT TO SHOW AN UNOBVIOUS DIFFERENCE

"[T]he PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product. Whether the rejection is based on inherency' under 35 U.S.C. 102, on prima facie obviousness' under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same...[footnote omitted]." The burden of proof is similar to that required with respect to product-by-process claims. *In re Fitzgerald,* 619 F.2d 67, 70, 205 USPQ 594, 596 (CCPA 1980) (quoting *In re Best,* 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977)).

MPEP 2112.01:

PRODUCT AND APPARATUS CLAIMS □ WHEN THE STRUCTURE RECITED IN THE REFERENCE IS SUBSTANTIALLY IDENTICAL TO THAT OF THE CLAIMS, CLAIMED PROPERTIES OR FUNCTIONS ARE PRESUMED TO BE INHERENT

Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433.

A REJECTION UNDER 35 U.S.C. 102/103 CAN BE MADE WHEN THE PRIOR ART PRODUCT SEEMS TO BE IDENTICAL EXCEPT THAT THE PRIOR ART IS SILENT AS TO AN INHERENT CHARACTERISTIC

Where applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection. "There is nothing inconsistent in concurrent rejections for obviousness under 35 U.S.C. 103 and for anticipation under 35 U.S.C. 102." *In re Best*, 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977). This same rationale should also apply to product, apparatus, and process claims claimed in terms of function, property or characteristic. Therefore, a 35 U.S.C. 102/103 rejection is appropriate for these types of claims as well as for composition claims.

The claimed compositions is not drawn to any particular hydrophobic group having linked to the modified RNA and not drawn to any amphipathic transfection reagent such as a lipid comprised within the composition, thus Fosnaugh et al. teach a product substantially identical to the claimed composition and the function or property of the modified RNA interacting with the transfection reagent via a hydrophobic interaction would be inherent. Moreover as evidenced by Thierry et al., liposomal complexes comprising oligonucleotides are formed by hydrophobic interactions (see generally columns 8-11).

Thus Fosnaugh et al. anticipates the instant claims.

Applicant argues that Fosnaugh et al. cannot anticipate the instant invention as Fosnaugh et al. do not teach a modified RNA wherein the RNA interacts with the

transfection reagent via hydrophobic interaction. This argument is not convincing because Fosnaugh et al. teach a product that is substantially identical to the claimed composition and thus the function or property of the modified RNA interacting with the transfection reagent via a hydrophobic interaction would be inherent. Moreover as evidenced by Thierry et al., liposomal complexes comprising oligonucleotides are formed by hydrophobic interactions (see generally columns 8-11).

Therefore Applicants arguments are not persuasive.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4-6, 10, 13 and 14 rejected under 35 U.S.C. 103(a) as being obvious over Fosnaugh et al. (US 2003/0143732 of record PTO Form 892 mailed 12/31/2007), Manoharan, M. (Biochimica et Biophysica Acta 1489, 1999: 117-130 of record PTO Form 892 mailed 12/31/2007) and further evidenced by Thierry et al. (US 6,110,490).

The instant claims are drawn to a composition for delivering an RNA to a cell comprising a reversibly modified RNA consisting of a hydrophobic group covalently linked to said RNA via a labile bond cleavable under mammalian physiological conditions and an amphipathic transfection reagent wherein the reversibly modified RNA and the transfection reagent associate to form a complex and wherein the

modified RNA interacts with the transfection reagent via hydrophobic interactions and drawn to a RNA that is modified and is selected from siRNA or microRNA, wherein the modified RNA is more resistant to nucleases and wherein a plurality of functional groups are attached to said RNA via labile bonds.

Fosnaugh et al. teach conjugates comprising siRNA and functional groups that are used to facilitate delivery of the siRNA into cells (see paragraph 0172). Fosnaugh et al. teach the siRNA can be modified at the 2' hydroxyl position (see paragraph 0165) and teach the functional groups are attached to the siRNA via biodegradable linkers wherein the linkers are degradable in biological systems i.e. mammalian cells (see paragraph 0174). Fosnaugh et al. teach the functional groups can be lipids, peptides, toxins or polymers that are capable of delivering the siRNA across cellular membranes, (see paragraphs 0172- 0175). Moreover, Fosnaugh et al. teach the conjugate can be delivered to an individual using liposomal delivery and teach standard protocols can be used for formation of the liposome complex (see at least paragraph 0195). As evidenced by Thierry et al., liposomal complexes comprising oligonucleotides are formed by hydrophobic interactions (see generally columns 8-11).

The claimed compositions is not drawn to any particular hydrophobic group having linked to the modified RNA and not drawn to any amphipathic transfection reagent such as a lipid comprised within the composition, thus Fosnaugh et al. teach a product substantially identical to the claimed composition and the function or property of the modified RNA interacting with the transfection reagent via a hydrophobic interaction would be inherent as stated above.

Manoharan et al. teach efficient conjugation of conjugates such as carbohydrates and other ligands at the 2' position of the RNA (see page 124).

It would have further been obvious to conjugate functional groups to RNA at the 2' hydroxyl position of the RNA, as taught by Manoharan. Further, one of skill in the art would have been motivated to attach the functional group to the 2' hydroxyl position of a RNA given Manoharan teach this position improves the chemical properties such as stability and nuclease resistance of said RNA molecules. Moreover, one would have expected to conjugate a functional group to the 2' hydroxyl position of a RNA give Manoharan et al. teach efficient RNA molecules with enhanced properties when functional groups are attached at the 2' position.

Thus in the absence of evidence to the contrary, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

Claim Rejections - 35 USC § 112

The rejection of claims 1, 4-6, 10 and 13-14 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn due to claim amendments.

Claim Rejections - 35 USC § 102

The rejection of claims 1, 4-6, 10 and 13-14 under 35 U.S.C. 102(e) as being anticipated by Fosnaugh et al. (US 2003/0143732 of record PTO Form 892 mailed 12/31/2007) as evidenced by Thierry et al. (US 6,110,490) is withdrawn in view of the new grounds of rejection above. Applicant's arguments are addressed above.

Claim Rejections - 35 USC § 103

The rejection of claims 1, 4-6, 10, 13 and 14 under 35 U.S.C. 103(a) as being obvious over Fosnaugh et al. (US 2003/0143732 of record PTO Form 892 mailed 12/31/2007), Manoharan, M. (Biochimica et Biophysica Acta 1489, 1999: 117-130 of record PTO Form 892 mailed 12/31/2007) and further evidenced by Thierry et al. (US 6,110,490) is withdrawn in view of the new grounds of rejection above. Applicant's arguments are addressed above.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful please contact the SPE for 1635 Heather Calamita at 571-272-2876. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

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/Kimberly Chong/
Primary Examiner
Art Unit 1635